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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
08/648,270	05/15/96	TOR	Y A-63463-1

EXAMINER

HM21/0617

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CRANE, L	PAPER NUMBER
ART UNIT	13

1623

DATE MAILED: 06/17/98

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 04/06/98

☐ This action is FINAL.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

- ☒ Claim(s) 1-25 is/are pending in the application.
Of the above, claim(s) 1-3, 6-8, 11 and 14-16 is/are withdrawn from consideration.
- ☐ Claim(s) _____ is/are allowed.
- ☒ Claim(s) 4-5, 9-10, 12-13 and 17-25 is/are rejected.
- ☐ Claim(s) _____ is/are objected to.
- ☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

- ☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- ☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
- ☐ The specification is objected to by the Examiner.
- ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- ☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been
- ☐ received.
- ☐ received in Application No. (Series Code/Serial Number) _____
- ☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e):

Attachment(s)

- ☒ Notice of Reference Cited, PTO-892
- ☒ Information Disclosure Statement(s), PTO-1449, Paper No(s) 10
- ☐ Interview Summary, PTO-413
- ☐ Notice of Draftsperson's Patent Drawing Review, PTO-948
- ☐ Notice of Informal Patent Application, PTO-152

18/684,270

SEE OFFICE ACTION ON THE FOLLOWING PAGES

* U.S. GPO: 1996-414-498/40517

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The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group 1600, Art Unit 1623.

5 No claims have been cancelled but claims **20-25** have been added as per the amendment filed April 6, 1998. Claims **1-3, 6-8, 11 and 14-16** have been withdrawn from consideration as being drawn to non-elected subject matter. Applicant will note that the instant amendment has been altered as provided for under 37 C.F.R.
10 § 1.126 to eliminate duplicate claims numbered **23**, i.e. claims **20-24** are now numbered **20-25**.

Claims **4-5, 9-10, 12-13 and 17-25** remain under consideration.

15 Claim **5** is rejected under 35 U.S.C. §112, fourth paragraph, as being of improper dependent form for failing to further limit the subject matter of a previous claim.

Instant claim **5** is improper because it depends from itself. (a new grounds of rejection).

20 Claims **4-5, 9-10, 12-13 and 17-25** are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

25 In claims **9, 10, 12, 13, 17, 18, 19, 20 and 21** the terms "comprising"/"comprises" and "further comprising" are incorrect as applied to a compound. Applicant is requested to note that claims

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directed to chemical compounds are indefinite when terms using variations of the verb "to comprise" are included, because consequently said terms imply the presence of other component parts which are not defined in the instant claims; e.g. metes and bounds are indeterminant.

Applicant's arguments filed April 6, 1998 have been fully considered but they are not deemed to be persuasive.

Applicant argues that the term "further comprising" is appropriate terminology in claim 13. Examiner respectfully disagrees. In compound claims, the term "comprising" or "further comprising" is inappropriate language in compound claims where the compound is of defined structure, i.e. structure is known and is not a component part of a larger structure, i.e. a control sequence is part of a complete DNA. It is inappropriate because the term "to comprise" is judicially recognized to mean "to include" which implies that there is more present than has been defined in the chemical structure. This is plainly inconsistent with a defined chemical structure with metes and bounds established by the chemical structure. If applicant argues that this is an inappropriate limitation because only a component is being claimed, applicant is referred to the new ground of rejection included herein under 35 USC §112, first paragraph which suggests that such an expansive view of the claimed subject matter brings up the issue of enablement.

Examiner is puzzled by applicant's view that claims 4 and 5 are "linking claims" and therefore they may include subject matter from non-elected inventions. This is not examiner's understanding of the meaning of the term "linking claims." As noted in the restriction, linking claims "will be examined to the extent they

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apply." In reality, applicant is expected to eliminate non-elected subject matter from linking claims during the prosecution of the elected invention. Applicant is encouraged to make the necessary changes to insure that non-elected subject matter has been
5 eliminated, and is requested to note that claims will not be allowed until such changes have been made.

In claims 4-5 it is unclear whether the instant claimed subject matter is properly included within the scope of the elected subject matter. Applicant is respectfully requested to more narrowly define
10 or more completely defined what is meant by the term "substituted aromatic group". Applicant is respectfully requested to limit the scope of the instant claims to the elected invention. The introduction of a Markush group is one way in which this might be accomplished; e.g. -- a substituted aromatic group selected from the group
15 consisting of nucleoside bases, nucleotide bases, and nucleic acid bases. --

Applicant's arguments filed April 6, 1998 have been fully considered but they are not deemed to be persuasive.

Applicant is respectfully requested to provide a more clearly
20 bounded definition of the instant subject matter. Applicant is respectfully requested to consider the suggestion made in the amended ground of rejection.

Claim 13 recite(s) the limitation "**M**", "**X**" and "**X₁**" in both the chemical formula provided and as defined variables. There is
25 insufficient antecedent basis for this limitation in in the parent independent claim, i.e. claim 12 fails to include these variables.

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Applicant will note that properly dependent claims must "further limit" the subject matter of claims from which they depend.

Applicant's arguments filed April 6, 1998 have been fully considered but they are not deemed to be persuasive.

5 Applicant's basic reliance on the term "comprising" is at the root of this problem. Compound claims may be configured with "consisting of" language to include all of the variables and variations in a base generic claim with subgeneric and species claims dependent therefrom. Applicant is encouraged to elect this claim drafting
10 strategy as the most effective approach to addressing the problems noted herein involving the inappropriate use of the term "comprising." See the Caruthers et al. '732 patent claims.

In claims **10 and 18**, the term "the phosphoramidite form of the nucleotide" suggests unfamiliarity with the terminology in the
15 instant art area. Applicant is referred to The Merck Index or any competent biochemistry text (Lehninger, etc.) and will therein find compounds such as "adenylic" and "guanylic" acids, which are monophosphates of adenosine and guanosine, respectively, aka "nucleotides" or "mononucleotides." Phosphoramidites, on the other
20 hand, are not typically referred to as nucleotides, as they contain phosphorus in a reduced form ($P^{(III)}$) which is not pharmaceutically useful, but is synthetically a commonly used intermediate in the preparation of oligonucleotides. Applicant may chose to replace the instant noted phrase in many different ways, but is particularly
25 encouraged to introduce chemical structures rather than names, so there is no doubt (indefiniteness) concerning the chemical structures being claimed.

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Applicant's arguments filed April 6, 1998 have been fully considered but they are not deemed to be persuasive.

Applicant's citation of two dictionaries and a biochemistry text is noted. Applicant is referred to the Caruthers et al. patents made of record to exemplify the parallels in claim structure when compound
5 claims ('732) and process claims('679) are making reference to compounds which are well defined (of known structure). Applicant note that the compound claims in the '732 patent do not rely on the term comprising. Applicant will also note that when process
10 claim.1 and claims dependent therefrom of the '679 patent make reference to compounds, narrow language and the attendant structure of the '732 patent are evident.

In claim 17, the term "comprises the base of a nucleotide" is indefinite and begs the questions i) which base or bases? and ii) at
15 what ring atom locations on each of the bases individually? For this reason the noted claim is incomplete in its description of the claimed subject matter.

Applicant's arguments filed April 6, 1998 have been fully considered but they are not deemed to be persuasive.

20 Applicant will note that the Caruthers et al. patents provide excellent examples of how to claim compounds generically. Applicant is encouraged to claim using complete generic structures in the claims which illustrate where the substitutions occur and leave little to the imagination concerning the metes and bounds of the claimed
25 subject matter.

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Claims **9, 10, 13, 17, 18, 19 and 21** are rejected under 35 U.S.C. 112, fourth paragraph, as being of improper dependent form for failing to further limit the subject matter of a previous claim.

5 In each of the noted claims, the term "comprising" (the only judicially recognized 'open' term) is used in a claim dependent from a claim wherein open language is not used. In addition each of the noted claims includes subject matter not specifically included within the independent claim from which it depends. Applicant is referred to the Caruthers et al. '732 patent for guidance on how to avoid this
10 difficulty in compound claim drafting.

Applicant's arguments filed April 6, 1998 have been fully considered but they are not deemed to be persuasive.

The above is a new ground of rejection.

15 In claim **19** applicant uses the term "nucleic acid" in a manner suggesting, but not clearly describing, modification of an oligonucleotide or a polynucleotide by incorporation therein of a compound of claim **12**. Inspection of claim **12** suggests that claim **19** is improperly dependent therefrom. In addition, claim **19** by its use of the term " comprising *the* compound according to claim **12** "
20 misuses the definite article (claim **12** is directed to a generic class of compounds; applicant may chose to substitute the term -- *a* --), and misuses the term "compound" when in fact a radical or diradical of one of the compounds of claim **12** is what is being included at an end of, or within the chain of, respectively, any one nucleic acid.

25 Applicant's arguments filed April 6, 1998 have been fully considered but they are not deemed to be persuasive.

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The above is a reformulation of an existing ground of rejection.

The following are all new grounds of rejection.

5 In claim 4, applicant has failed to provide sufficient definition either within the claim or within the disclosure to define where the substituent "Z" is attached to the alkynyl moiety when Z is defined as a nucleoside, a phosphoramiditylated nucleoside, a nucleotide or a nucleic acid.

In claim 5, the term "Z" has not been defined thereby rendering the notes claim incomplete.

10 Claims 9 and 20 are duplicates. Applicant is respectfully requested to cancel one of the noted claims or take other appropriate action.

15 In claim 10, the term "the phosphoramidite form of the nucleoside" represents internally inconsistent use of chemical terminology. Did applicant intend -- wherein Z represents a nucleoside-base-derived radical and is further modified by the attachment of a 2'-, 3'- or 5'-phosphoramidityl moiety --? The same problem occurs in claim 18.

20 In claim 12, line 5, the term "A and B are selected from carbon or nitrogen such that Y is a bond selected form the group consisting of acetylene, alkene, azo or imine" is unclear by improper and/or incomplete use of chemical terminology. Applicant has failed to provide complete structural/stereochemical information and substitutions when the AYB linkage is with an alkenyl or a imino
25 moiety. In addition, the terminology wherein a bond is described in

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terms normally reserved for generic classes of compounds is unclear, e.g. did applicant intend to include a "diazo {-N=N-}" linkage? An alternative and less confusing way to phrase this part of the claim would be -- A-Y-B represents a two atom linkage with variable
5 bonding represented by Y and the entire moiety may be selected from the group consisting of 1,2-alkynyl; 1,2-(*cis* or *trans*)-alkenyl, 1,2-(*cis* or *trans*)-diazo; or imino wherein the remaining substituents of the alkenyl linkage are selected from the group consisting of ... and the remaining substituent of the imino linkage is selected from the
10 group consisting of ... --. This suggested language also reveals missing information and suggests that applicant's disclosure is defective. In order to insert the limitations represented by " ... " applicant would have to introduce new matter into the disclosure.

In claims 17-19, the term "the base of a ..." (emphasis added)
15 represents incorrect use of the definite article. As reference is being made to generic claims which define sets of many different compounds, applicant is respectfully requested to refer to each individual compound alternative by substitution of the indefinite article -- a -- in each of the noted claims. The same problem
20 reoccurs in claims 9-10, 20-21.

In claims 22-25 applicant lists the nucleosides "adenosine, guanosine, thymidine, cytidine and uridine" thereby suggesting that applicant's intention is to limit claimed analogues to those derived from the four most common RNA nucleosides (A, G, C and U) and
25 only one DNA nucleoside (T, aka 5-methyl-2'-deoxyuridine). Examiner points this out only to make clear that applicant's choice of this subject matter limitation is very unusual.

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In claims 22-25, the term "said base is selected from adenosine, guanosine, thymidine, cytidine and uridine" includes incorrect use of chemical terminology. Did applicant intend -- said base-linked nucleosidyl moiety is selected from adenosinyl, guanosinyl, thymidinyl, cytidinyl and uridinyl -- ? In nucleic acid parlance the term "base" refers to the N-heterocyclic substituent of a nucleoside (e.g. 9-adeninyl) or the compound derived therefrom (e.g. adenine). The nucleosides named above are each complete individual compounds, not chemical substituents (e.g. "adenosine" is also known as '1-(9-adeninyl)-ribose').

Claims 4-5, 9-10, 12-13 and 17-25 are rejected under 35 U.S.C. §112, first paragraph, as the disclosure is enabling for certain non-nucleoside/nucleotide/nucleic acid containing compounds only. See MPEP §§706.03(n) and 706.03(z).

The instant specification has disclosed chemical structures of some compounds which are encompassed by the instant claimed invention, but said specification has not disclosed either how to make or how to use these phenanthroline-linked-nucleosides, -nucleoside phosphoramidites, -nucleotides, or -nucleic acids. Examiner does not doubt that applicant as well as the ordinary practitioner may be able to practice the claimed invention, i.e. make the claimed monomeric compounds and incorporate same in a nucleic acid. However, examiner does not think the instant specification is sufficiently detailed to provide the necessary guidance to achieve this end without undue experimentation. It is well known and established that the "law requires that disclosure in an application shall inform those skilled in the art how to use appellant's alleged discovery, not

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how to find out how to use it for themselves." *In re Gardner et al.*,
166 USPQ 138 (CCPA 1970).

Applicant's arguments filed April 6, 1998 have been fully
considered but they are not deemed to be persuasive.

5 The above is a new grounds of rejection. Examiner notes the
complete absence of any "Examples" wherein the synthesis, or use in
subsequent syntheses, of any one of the compounds claimed herein
(nucleoside analogues, nucleoside phosphoramidites, nucleotide
analogues, or nucleic acids with phenanthrolinyl moieties attached)
10 are described.

Papers related to this application may be submitted to Group
1600 via facsimile transmission(FAX). The transmission of such
papers must conform with the notice published in the Official Gazette
(1096 OG 30, November 15, 1989). The telephone numbers for the
15 FAX machines now operated by Group 1600 are **(703) 308-4556**
and (703) 305-3592 for Official documents. Before transmission of
any Draft communications, Applicant is respectfully requested to seek
instructions from instant Examiner.

Any inquiry concerning this communication or earlier
20 communications from the examiner should be directed to Examiner L.
E. Crane whose telephone number is 703-**308-4639**. The examiner
can normally be reached between 9:30 AM and 5:00 PM, Monday
through Friday.

If attempts to reach the examiner by telephone are unsuccessful,
25 the examiner's supervisor, Marian Knode, can be reached at (703)-
308-1235.

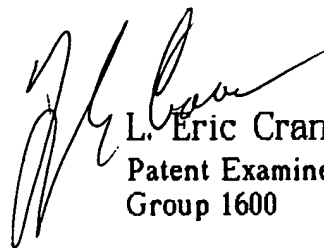
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Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is 703-**308-1235**.

5 LECrane:lec
6/11/98



L. Eric Crane
Patent Examiner
Group 1600